

THE JOINT UNITED NATIONS PROGRAMME ON HIV/AIDS (UNAIDS)

BEST PRACTICE

**PREVENTION OF MOTHER-TO-CHILD
TRANSMISSION OF HIV:
THAI RED CROSS ZIDOVUDINE
DONATION PROGRAMME**

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Bangkok, Thailand

SEPTEMBER 2000

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INTRODUCTION

Over the past decade, The HIV/AIDS epidemic in Thailand has grown from a handful of infections to a major public health problem with tremendous medical, psychosocial and economic consequences for the country. The infection initially spread among homosexual men and injecting drug users before it gained a foothold among commercial sex workers. It then swiftly spread from commercial sex workers to their clients and subsequently to the clients' spouses or partners and finally their children.

While intervention efforts may have slowed the spread of HIV in Thailand, this cannot alter the fact that a large number of people who have the virus do not have any symptoms for a long period of time and are therefore not aware of their infection status. Hence, a large reservoir of the virus remains in the community and the epidemic spread of HIV continues. It has been estimated that approximately one million Thais (1.9 per cent of population) are infected with HIV nationwide. In some parts of the country, the infection rates are much higher. Since heterosexual transmission is the most frequent mode of transmission in Thailand, Thai women are obviously at risk for contracting this disease. Once the women are infected and become pregnant, they can transmit the virus to their unborn children.

A survey in 1998 by the Thai Ministry of Public Health found that approximately 1.5 per cent of pregnant women attending at antenatal care clinics were HIV-infected. Based on this finding, it is predicted that 15,000-20,000 HIV-infected women will give birth every year. Since the transmission rate of HIV from pregnant Thai women to their infants is between 19 to 25 per cent, about 3,000-5,000 HIV-infected Thai children would be born annually if no interventions were implemented.

HIV-infected children frequently experience many medical and psycho-developmental complications as the result of the infection. These lead in many cases to impaired development, multiple and prolonged hospitalizations and early death. The devastating impact is not limited only to the infected child. The family or the guardian will be greatly affected, both psychologically and socio-economically, by the child's illness. The impact will eventually extend to the community in many ways. The community will be affected by the direct and indirect cost of the child's medical care. Household members will not be able to participate in the workforce at the same level, as they are obliged to take care of the sick child. The problems of discrimination and the curtailment of educational opportunities will ultimately arise. Therefore, any interventions that can reduce the number of HIV-infected Thai children are certainly worthwhile and will benefit the society.

In 1994, the landmark Paediatric AIDS Clinical Trials Group (ACTG) 076 study in the United States and France demonstrated that zidovudine, a medication against HIV, can reduce the risk for mother-to-child transmission of HIV by almost 70 per cent. This intervention was quickly adopted as the standard of care in most developed countries and it has contributed to the significant reduction of paediatric HIV/AIDS cases in those countries. However, because of its high cost and complexity, it is impossible to implement this strategy in most of the developing world.

BRIEF DESCRIPTION OF THAI RED CROSS ZIDOVUDINE DONATION PROGRAMME

The Thai Red Cross zidovudine donation programme was contrived by the Thai Red Cross AIDS Research Centre of the Thai Red Cross Society. In brief, the programme procures zidovudine for HIV-infected pregnant women by means of public donation. The donation can be in the form of either the medication or financial support. By using the donated funds, the Thai Red Cross can purchase zidovudine in a large quantity at low cost. The medication is distributed throughout the country upon the request of pregnant women's health care providers.

After a pregnant woman has been provided with voluntary counselling and testing, and has been tested positive for HIV, her health care provider can request zidovudine for her from the Thai Red Cross.

Once the request is approved, the medication will be delivered to the health care provider periodically.

The zidovudine supply will be sufficient for a pregnant woman and her infant according to the prophylactic regimen, which should be started any time between 14 and 34 weeks' gestation and should be continued until delivery. The infant will receive zidovudine during the first 6 weeks of life.

The health care provider taking care of the infant is asked to submit infant's dried blood spots on the provided filter paper to the Thai Red Cross. These blood samples are to determine whether the infant acquires HIV from the mother. The test result is made available to the health care provider, who will inform the parents of their child's infection status. The medication, the medication shipment and the blood testings are all provided at no cost to the family or the health care provider.

OBJECTIVES OF THE PROGRAMME

The objective of this programme is to procure zidovudine with public donations and to provide it at no cost to HIV-infected pregnant women throughout Thailand who cannot afford this medication. The programme's major goal is to reduce the number of Thai children being infected with HIV from their mothers. This objective genuinely follows the basic principle of the Red Cross as being a charitable, non-profit, humanitarian organization.

BRIEF HISTORY OF THE PROGRAMME

PHOTO #1 THE PRINCESS IS HOLDING AN INFANT

Caption: On World AIDS Day, Her Royal Highness Princess Soamsawali was carrying an infant born to an HIV-infected mother, who participated in the zidovudine donation programme.

In early 1996, the administrative members of the Thai Red Cross Society were honoured to meet with Her Royal Highness Princess Soamsawali. The problem of HIV infection in Thailand was the main topic of discussion at that meeting. Her Royal Highness addressed her concerns about the alarming number of Thai children born to HIV-infected mothers and how the children and the families suffer from this devastating disease. At that time, the zidovudine regimen according to the ACTG 076 study was already proven to be effective in reducing HIV transmission from mothers to infants if given during pregnancy, during labour and to the infant after birth. A shorter and less expensive zidovudine regimen was being evaluated in several clinical studies but the results would not be available for the next few years. Due to the high cost of the zidovudine (ACTG 076) regimen, most Thai women could not afford it. Her Royal Highness envisioned that the only way HIV-infected pregnant women would have an immediate access to the medication was through public donation and suggested that the Thai Red Cross was in the proper position to initiate such a programme.

In response, the Thai Red Cross AIDS Research Centre, formerly known as the Programme on AIDS of the Thai Red Cross Society, took on the responsibility of setting up the zidovudine donation programme for HIV-infected pregnant Thai women. Her Royal Highness Princess Soamsawali graciously accepted the role of patron of the programme, which began on the 26th of February 1996. In addition, Her Royal Highness was the first donor who provided funds for this programme, which has grown tremendously since its inception.

MAJOR ELEMENTS OF THE PROGRAMME

AN OPTION FOR MOTHERS-TO-BE

PHOTO #2 A PREGNANT THAI WOMAN WITH HER COUNSELLOR

Caption: An HIV-infected pregnant woman is discussing her options with a counsellor.

With assistance from the Thai Ministry of Public Health, all hospitals throughout Thailand were informed of this programme. In addition, the mass media have provided the public with information on this programme through newspapers, pamphlets, magazines, and radio and television broadcasts. All these tasks on public notification have been succeeded with the help of the Thai Red Cross public relation and fundraising committees.

The health care provider who takes care of an HIV-infected pregnant woman can request zidovudine directly from the Thai Red Cross. It is suggested that the health care provider should discuss the following issues, which appear as a checklist on the drug request form, with the woman and her spouse prior to requesting the medication:

- The risks of HIV transmission from her to her unborn child and the choices of intervention
- The benefit of zidovudine in the prevention of HIV transmission
- The adverse side effects of zidovudine
- The mode of taking the medication and the woman's willingness to receive and take this donated medication
- The risk of HIV transmission through breast feeding and the family's access to formula feeding
- The way to determine the child's HIV status and the couple's willingness to bring their child for testing and for medical follow-up.
- The couple's intention to raise the child
- The decision on a surrogate guardian for the child once the couple can no longer take care of the child in the future
- Appropriate family planning after the current pregnancy

The health care provider should inquire about the family income and occupation so that the donated medication is appropriately offered only to those who truly cannot afford it. The physician should emphasize to the couple of the risk for HIV transmission through breast-feeding. The Thai Red Cross advocates that breast-feeding by HIV-infected women be discouraged. Alternative feeding should be thoroughly discussed with the couple. More than one counselling session may be required. At all times, the health care provider must assure the couple that their discussion will be based on the element of confidentiality and that the couple's decision will be respected.

A MISSION TO SAVE THE CHILD'S LIFE

After all the discussions have taken place and the woman has accepted to take zidovudine, the health care provider fills out the drug request form. The information needed in this form includes the family demography, family income and occupation, the history of pregnancy, the counselling checklist as above, the hospital address to which the medication should be delivered and the health care provider's name and signature. This form ensures that all the important information has been discussed with the patient and provided to the Thai Red Cross. However, no patient's names are recorded on this form. The drug request form is then sent to the Thai Red Cross preferably by facsimile. The process of approval usually takes no more than one week. Once the request is approved, the health care provider will be notified. Zidovudine is usually delivered within two weeks after notification. The first shipment will be sufficient for one patient to use for 3 months. Subsequent follow-up forms are to be filled out so that the medication can be delivered continuously to complete the whole course of the prophylactic regimen.

The zidovudine regimen used in this programme is as follows:

1. During pregnancy, a woman starts taking zidovudine any time between 14 and 34 weeks' gestation. The daily dose is 200 milligrams of zidovudine (2 pills) in the morning and 300 milligrams (3 pills) in the evening until the woman goes into labour.

2. During labour, a woman takes 300 milligram of zidovudine (3 pills) by mouth every 3 hours until the infant is born.
3. After birth, the infant takes zidovudine syrup at the dose of 2 milligrams per kilogram body weight every 6 hours until the infant is 6 weeks old.

This regimen is somewhat different from the ACTG 076 regimen. In the ACTG 076 regimen, a woman would receive 100 milligrams of zidovudine five times daily during pregnancy. In this programme, the dosing of zidovudine is less frequent for better compliance. In addition, zidovudine was given intravenously (given into a vein) during labour in the ACTG 076 study. However, giving medication intravenously can be quite complicated, especially in some community hospitals in rural Thailand. Therefore, it was decided to give the medication by mouth at every 3 hours instead. It was found that the zidovudine level in the body remains quite comparable regardless of whether the medication is administered orally or intravenously.

NEW LIFE FOR THE CHILD

The Thai Red Cross provides HIV testing free of charge for all infants who receive zidovudine from the programme. Upon the parent's permission, blood samples are obtained by a heel stick or finger stick technique. We recommend that blood samples be obtained at birth, at 6 weeks and at 6 months of age. Small drops of blood are placed on the provided filter paper and allow to air-dry. The samples are then mailed with the corresponding form to the Thai Red Cross in the envelope provided.

At the Thai Red Cross Laboratory, the dried blood spot samples are analysed for HIV. The technique used is called the polymerase chain reaction assay. In brief, the HIV gene is amplified if it is present in the dried blood spot. The gene is subsequently detected using a standard laboratory technique. This method has proved sensitive and specific for the diagnosis of HIV infection in infants. Once the result is available, the health care provider will be notified so that the parent will be informed of the child's HIV infection status. The Thai Red Cross encourages that all children born to HIV-infected mothers be

tested for HIV antibody at least once at or after the age of 15-18 months to confirm the child's infection status. This recommendation is included in the last form as a reminder.

DONATION CAMPAIGNS

Photo #3 SIX PERSONS IN THE PICTURE

Caption: The Red Cross Red Ribbon Sale and the exhibition of the zidovudine donation programme

Photo #4 PEOPLE ON BICYCLES

Caption: A campaign activity at King Rama V Square to raise public awareness and support on the anniversary of the zidovudine donation program

All zidovudine used in this programme comes from public donations. The donation campaign is under the direct responsibility of the public relation and fundraising committees of the Thai Red Cross. These committees consist of volunteers from various walks of life - from chief executive officers to entertainers and from royal family members to government officers. The donations are obtained through four different ways as follows:

1. Direct donation

This is the major source of the programme's fund. The Thai Red Cross accepts donation year-round from individuals, groups or organizations. The mass media regularly publicize the need for donations. One can donate in person at the Red Cross offices, by sending a cheque or a money order, or by transferring funds to the programme's bank account. There are no limits on the amount of donation. In addition, the donation is tax-deductible.

2. Donation through the Thai Red Cross annual activities

With the effort of the public relation and fundraising committees, the Thai Red Cross has many activities for the general public each year. The main activities or events for example are the Annual Thai Red Cross Fair, the World AIDS Day activities, the National Mother's Day celebration, and the Princess Soamsawali's birthday celebration. On these special occasions, other than the donation

campaign, there are countless educational activities related to HIV/AIDS prevention and care. This helps contribute to a better understanding of HIV/AIDS within the Thai society.

3. Donation through the Red Cross Red Ribbon Sale

Every year on 26 February, in recognition of the day this programme was founded, the Thai Red Cross holds the Red Cross Red Ribbon Sale throughout Thailand. This event, which is dedicated to those who suffer from AIDS, seeks to raise public awareness of this disease. Parts of the profit are directed to the zidovudine donation programme.

4. Donation through miscellaneous activities

The public relation and fundraising committees have worked with several non-government organizations and the private sectors to establish a variety of fundraising activities. These include charity concerts, dinners, fashion shows, golf tournaments, gallery exhibitions, and the sale of special cassettes or compact discs, and so on.

PARTNERSHIPS AND ALLIANCES

THE ROLES OF THE ROYAL FAMILY

As its patron, Her Royal Highness Princess Soamsawali has taken an active role in guiding and overseeing the zidovudine donation programme. Her Royal Highness has devoted her time to participate in numerous events related to this programme, has chaired the programme's annual meeting, and has regularly donated funds and infant formula for the programme. One main event is the Spiritual Candle Light Ceremony on the World AIDS Day, when Her Royal Highness specifically meets with patients, volunteers and those who work in the field of HIV. On Her Royal Highness's birthday, there are abundant activities related to HIV/AIDS throughout the country. As the result of her dedication, Her

Royal Highness has been acknowledged, both by Thai and by the international community, including UNAIDS and UNICEF, as the foremost figure in HIV prevention and education in Thailand.

Her Royal Highness Princess Soamsawali is not the only royal family member involved with the Thai Red Cross. Her Royal Highness Princess Maha Chakri Sirindhorn is the patron of the Thai Red Cross Society. Although Her Royal Highness may not have an active role in the zidovudine donation programme, Her Royal Highness oversees all activities of the Thai Red Cross Society, including those related to HIV/AIDS, and has provided valuable inputs for the operation of the Thai Red Cross AIDS Research Centre. In addition, parts of this programme's fund have come directly from Her Royal Highness's donations.

MINISTRY OF PUBLIC HEALTH

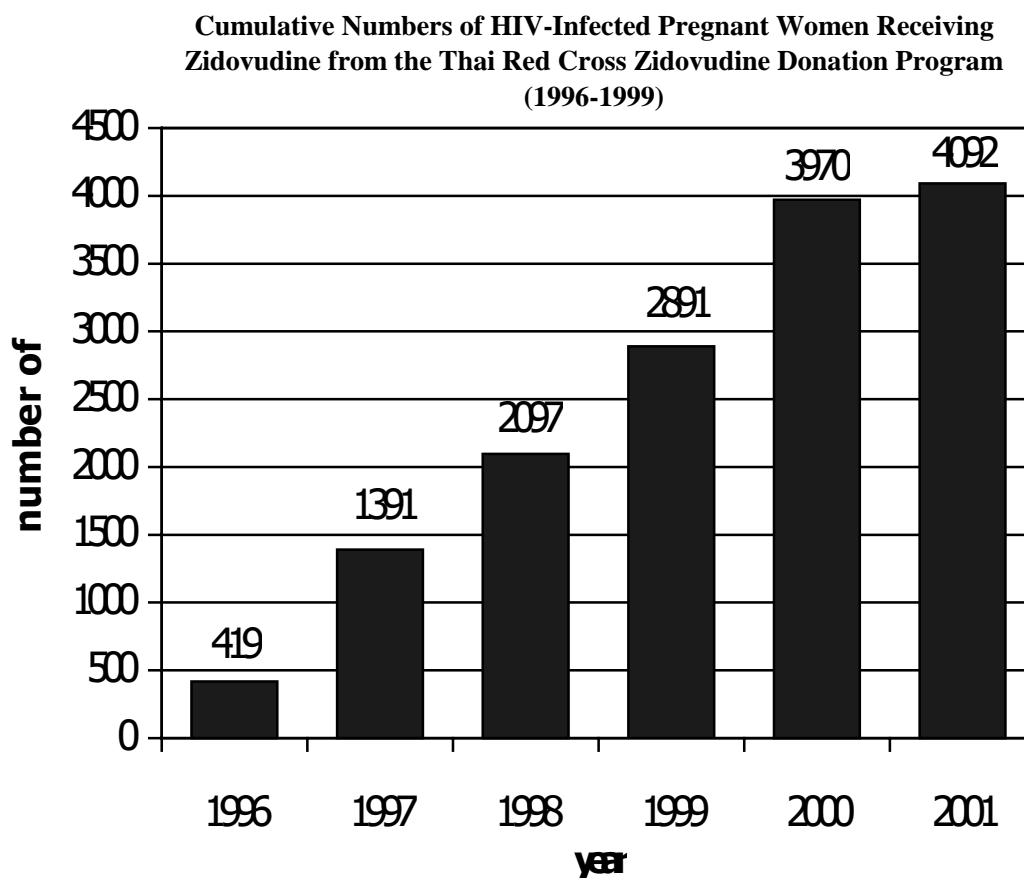
The Thai Ministry of Public Health, particularly the Division of AIDS, has played an important role by providing information on the programme to all hospitals throughout the country. The Ministry has helped streamline the process by which hospitals participate in the programme, and it continues to monitor and evaluate each hospital's participation. Such intervention has helped tremendously in the smooth operation of the programme at these hospitals. In addition, the Ministry has contributed zidovudine to be used in the programme.

PUBLIC SUPPORT

One reason that explains the success of this programme is its 'community-to-community' nature. The donation from the community eventually returns back to the community. Being Buddhists, Thai people strongly believe that it is religiously important to support charities. Preventing one child from this deadly disease is considered by Thai as one of the most favorable and charitable attainments. Therefore, the programme is very well received and fits very well in Thailand.

MONITORING AND EVALUATION

From February 1996 to August 1999, there had been almost 2,900 HIV-infected pregnant women receiving free zidovudine from this programme (see graph). They were from 81 hospitals in 40 provinces throughout Thailand. The analysis of the transmission rate was performed by the Thai Red Cross in August 1999. The analysis was limited to a subgroup of 719 mother-infant pairs among whom dried blood spot HIV tests were available on infants at or after 4 weeks of age. The mothers started zidovudine during pregnancy at 14-34 weeks' gestation and continued till delivery, and the infants received zidovudine for 6 weeks after birth. The transmission rate in this group was 5.9 per cent, which is agreeable with the rates reported from developed countries where zidovudine ATCG 076 regimen was implemented. Therefore, the scientific strength of this programme exists as it is now proven that zidovudine remains effective in reducing mother-to-child transmission of HIV outside the setting of clinical research in the less-developed region of the world. Our analysis also confirmed that zidovudine is effective in the population with predominant HIV subtype E infection. Of note, HIV subtype E is the most common subtype in Thailand whereas subtype B is the most common subtype in the western world. The ACTG 076 study was performed in the United States and France where HIV subtype B is predominant.



This programme has demonstrated that the community can work effectively together to overcome the obstacle of the high cost of zidovudine. Donation of medication has proved feasible and can be used as one of the strategic tools to prevent mother-to-child transmission of HIV in less-developed countries.

LESSONS LEARNED

Because the HIV/AIDS epidemic continues in Thailand, the Thai Red Cross foresees the necessity of maintaining the zidovudine donation programme. Several plans, with some modification, have been laid out for the continuation of the programme.

We have recently analysed the data from this programme. The analysis showed that the transmission rate in women who received zidovudine less than or equal to 8 weeks before delivery was not statistically different from the transmission rate in those who received zidovudine more than 8 weeks before delivery (3.4 per cent and 6.5 per cent, respectively). In response to this finding, by late 1999 the Thai Red Cross advised that antepartum zidovudine for pregnant women in this programme should be started at 32 weeks' gestation and be continued till labour. This will help save the fund and the medication without compromising the effectiveness of the regimen, enabling the programme to provide the medication to more women. The intrapartum and the neonatal components of this prophylactic regimen remain unchanged. Periodic assessments have taken place thereafter to assure that the transmission rate remains within an acceptable range.

Since the medical knowledge in the field of HIV evolves rapidly, the Thai Red Cross recognizes that this programme may need to be frequently updated to provide the greatest benefit to patients. A recent study from Uganda (HIVNET 012) compared the safety and efficacy of nevirapine with zidovudine in the reduction of mother-to-child transmission. Both medications were well tolerated with no different adverse events observed in both groups. The transmission rate was almost 50 per cent lower among those receiving nevirapine compared with those receiving the short-course zidovudine. This new information has led the Thai Red Cross to develop a new intervention strategy. In the year 2000, nevirapine as described in HIVNET 012 study will be incorporated into the programme's regimen. Both zidovudine and nevirapine will be offered to all participating pregnant women and infants. Theoretically, using both medications together to tackle the virus may lead to further reduction of transmission.

The zidovudine donation programme has proved feasible and successful in the Thai setting. The next step that the Thai Red Cross plans is to communicate with hospitals that have not yet taken part in this programme. In addition, the Thai Red Cross has recently been made a UNAIDS collaborating centre. This will expand the role of the organization in this region. The model of this programme can possibly

be used as a demonstration or a prototype for other countries in this region.

Despite its clear effectiveness, the programme has some weakness as follows:

- Although the health care providers are asked to return all follow-up forms, this is not mandatory in practice. Many patient forms were missing. This makes a retrospective assessment difficult.
- There is no direct information on patient's adherence to the medication and to the medical follow-up. Without complete and accurate information, it is difficult to evaluate all aspects of the programme.
- Giving the nature that the programme is not a research project, some health care providers therefore did not send the infants' dried blood spots for HIV testings. It is possible that some infants may not have been brought in for follow-up, some families may have relocated, and some infants may have been tested locally by their primary care physicians.
- Although the programme has been publicized for almost 4 years, some antenatal care facilities may not be aware of it. As a consequence, the pregnant women may not be adequately counselled, the decision to participate may not be appropriately reached and zidovudine prophylaxis may not be properly offered.
- Whereas the programme focuses on reducing the number HIV-infected children, the future of the uninfected children is not addressed, particularly the issue of orphaning. In addition, there are no set medical care plans for the infected parents. Multidisciplinary approaches are absolutely necessary to solve the problems of this magnitude.

Although no formal evaluations have taken place, the Thai Red Cross periodically arranges a meeting with all participating hospitals. The discussions are generally focused on the problems that health care providers and the Thai Red Cross have faced and how to solve them. This has led all parties to a better understanding and cooperation, which ultimately benefits pregnant women and children.

BEST PRACTICE

RELEVANCE

The programme's main objective is to make zidovudine accessible for HIV-infected Thai women with help from the community. The spread of HIV/AIDS in Thailand is mostly by heterosexual transmission. The increasing number of HIV-infected women has led to a large number of children born with this disease. Without interventions, the country will have to face with a significant number of paediatric HIV cases. The medical care for these children will be very costly and may well be a burden for the country. Therefore, every effort must be made to reduce the number of those affected children. This programme concentrates on providing free zidovudine to prevent transmission of HIV from pregnant women to infants and it should be considered as one of the options for these women. This initiative should be viewed as a pilot project. With respect to convincing the society that intervention strategies can be implemented even in the resource-poor setting, it has been successful.

EFFECTIVENESS AND EFFICIENCY

The programme is administered by the Thai Red Cross AIDS Research Centre headed by the Thai Red Cross Society. Since this is not a research project, the administration structure is organised to be efficient while maintaining flexibility in operations. The programme has set certain criteria in an attempt to ensure that zidovudine will be offered to those who are truly unable to afford the medication. This has met the donors' expectation that the funds or the medication they donate should go to those who really need it. It also ensures that the programme will not be abused.

The programme, with the help from the public relation and fundraising committees of the Thai Red

Cross, has invited participation from the public and private sectors in both publicizing this programme and providing financial support. This kind of cooperation has continued to grow.

As was previously mentioned, the effectiveness of this programme has been reflected by the low transmission rate of 5.9 per cent. The programme and its results were recently presented at the Second Conference on Global Strategies for the Prevention of HIV Transmission from Mothers to Infants in Canada.

ETHICAL SOUNDNESS

This programme is operated by the driving force of charity and humanity from the community. The medication that the Thai Red Cross purchases is used exclusively for the programme. Moreover, no request has ever been rejected and we believe that the medication is equally allocated to all. The existence of this programme has stimulated health care providers in Thailand to include the discussion of HIV as a relevant health concern for every pregnant woman and to offer the voluntary counselling and testing services. The programme has also set the standard of care for HIV-infected pregnant women and has helped shape the direction and the ethics of the clinical research on mother-to-child transmission in this country and in the developing world.

SUSTAINABILITY

This programme has been operating for almost 4 years. Judging by the number of request, the level of donations, and the amount of the medication allocated each year, it is evident that there is a continuing need for this programme. However, it needs to be kept up-to-date with the new medical and social information. We believe that as long as HIV/AIDS remains a public health problem for Thailand, the 'community-to-community' programme of this kind must exist. It could be one of a few weapons that the society has to combat and control this deadly disease.

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